Conformational Study of *cis*-Cyclononene by Dynamic NMR Spectroscopy and Computational Methods

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The ^{13}C NMR spectrum of the olefinic carbons of *cis*-cyclononene (**1**) at −189.3 °C showed three peaks, still exchange-broadened, which were interpreted in terms of two conformations. Relative free energies of conformations were estimated from ab initio calculations at the HF/6-311G* level and molecular mechanics (MM3) calculations, and possible assignments were made on the basis of these calculations and the experimental data. The major conformation has C_1 symmetry and a population of 66% at −189.3 °C. The structure suggested to be the minor conformation also has C_1 symmetry, but the deviation from C_s symmetry is small, resulting in a time-averaged plane of symmetry, even at −189.3 °C. Free-energy barriers of 4.18 ± 0.15 and 4.28 ± 0.15 kcal/mol for interconversion of the two conformations at −183.1 °C were calculated from the rate constants derived from line shape matching of the ^{13}C spectrum of the olefinic carbons at this temperature. Major-to-minor free-energy barriers for four temperatures from −178.3 to −189.3 °C were within the range of 4.28 to 4.35 kcal/mol. Interconversion of sites within the major conformation occurs through conversion to the minor conformation. The effects of a second process were observed in the ^{1}H NMR spectra of the allylic protons of **1**. Two multiplets of equal intensity were found by −124.8 °C, and a free-energy barrier of 8.05 ± 0.2 kcal/mol was calculated at coalescence (−102.3 °C). The changes were suggested to be due to slowing the exchange of geminal hydrogen positions.

Introduction

The conformations and barriers to conformational changes of the cycloalkenes are of interest for comparison with these properties of cycloalkanes and related compounds. Eclipsed butane segments are generally avoided in the low-energy conformations of cycloalkanes, but a CCCC dihedral angle near 0° is required for the double bond of a *cis*-cycloalkene. For this reason, it is expected that the preferred conformation of a *cis*-cycloalkene may be different from that of the corresponding saturated compound.

Cyclohexene adopts the half-chair conformation,[1] but the corresponding conformation of cyclohexane is a transition state for ring inversion of the chair form and has a free energy of more than 10 kcal/mol, relative to the chair.[2] The chair conformation is preferred by cycloheptene,[3] but cycloheptane exists in the axis-symmetrical twist-chair conformation, which is about 1.0 kcal/mol lower in strain energy than the chair.[4] The preferred conformations of cyclooctane and cyclodecane are the boat-chair[5] and boat-chair-boat,[6] and similar conformations were found at low temperatures for *cis*-cyclooctene[7] and *cis*-cyclodecene,[8] with the double bond of the alkene replacing a central bond of the boat part of the cycloalkane.

Strain energies for the conformations of *cis*-cyclononene (**1**) and free energies at two temperatures have been calculated by molecular mechanics with Allinger's MM3 force field,[9] but experimental studies have not been described. We report here the results of low-temperature ^{1}H and ^{13}C NMR studies of **1**. Also, free energies at room temperature and −189.3 °C were calculated by both force-field (MM3) and ab initio methods.

Experimental Section

cis-Cyclooctene, carbon tetrabromide, and methyllithium were purchased from Aldrich Chemical Co., and high purity propane was obtained from MG Industries, Morrisville, PA. 1,2-Cyclononadiene was synthesized from *cis*-cyclooctene, carbon tetrabromide, and methyllithium,[10] and part of the excess cyclooctene was removed by distillation of the product under reduced pressure. Treatment of the allene with sodium and ammonia gave *cis*-cyclononene[11] which was purified by vacuum distillation, followed by preparative gas chromatography with a 1/4 in. × 4 ft column containing 20% carbowax on 80/100 chromosorb P. A column temperature of 100 °C was used. The purity level was established by the room-temperature ^{13}C and ^{1}H NMR spectra.

A 10% solution of **1** in propane was prepared in a 5 mm thin-walled NMR tube, which was kept below 0 °C most of the time. *Caution*: high pressure. A small amount of TMS was added to provide an internal reference. NMR spectra were recorded on a General Electric Model GN-300 wide-bore NMR spectrometer, operating at a frequency of 75.57 MHz for carbons and 300.52 MHz for protons. Spectra were taken with a 5 mm dual probe, and spinning was discontinued below about −120 °C. The sweep width, pulse width, tip angle, and block size were ± 10 500 Hz, 6 μs, 60°, and 64 K for carbons and ±

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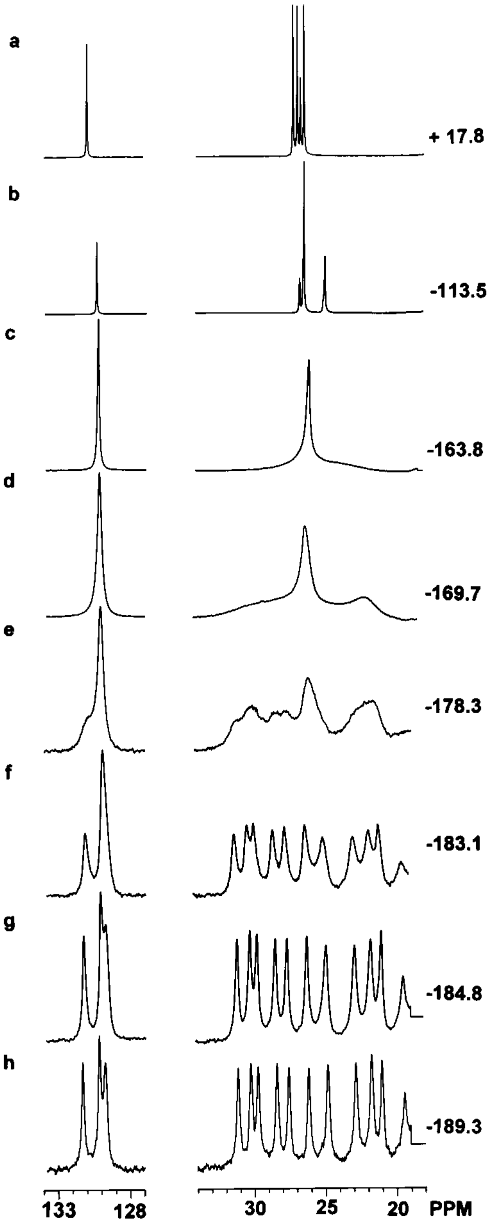

Figure 1. Low-temperature ^{13}C NMR spectra of *cis*-cyclononene in propane.

3000 Hz, 4 μs, 45°, and 64 K for protons. For the ^{13}C spectra, the delay times between pulses were 12 s at +17.8 °C and 1 s at all other temperatures. A delay time of 5 s was used for the ^{1}H spectra. Line broadening of 3.0 Hz was used to increase the signal-to-noise ratios for the ^{13}C spectra; the number of acquisitions for these spectra varied from 42 to 1200.

Because of the difficulty in ejecting the sample at lower temperatures, the temperature calibration was performed separately, using a copper–constantan thermocouple immersed in the same solvent contained in a nonspinning dummy sample tube and under conditions as nearly identical as possible, including the gaseous nitrogen pressure and flow rate and the level of liquid nitrogen in the Dewar which was used for cooling the coil. The emf's were measured with the decoupler off and using a Leeds and Northrup Model 8690-2 millivolt potentiometer. The uncertainty in the temperatures was estimated to be ±2 °C.

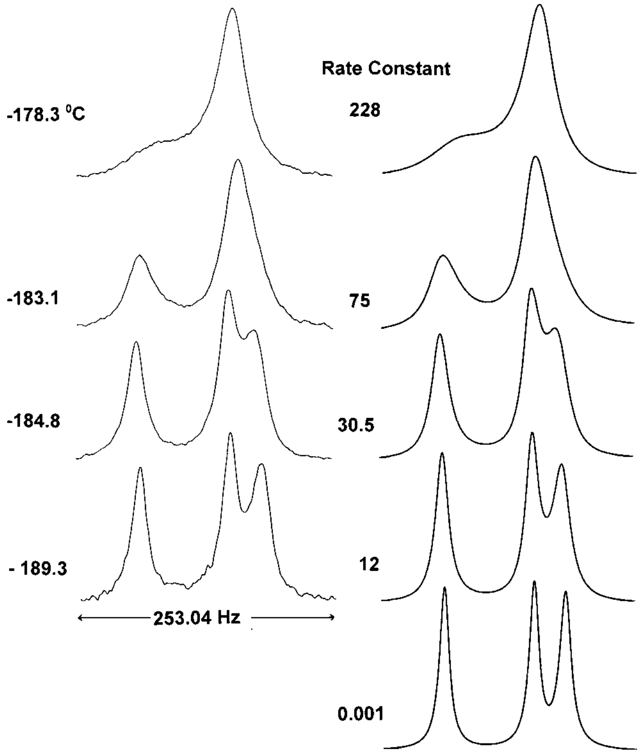

Figure 2. Experimental (left) and calculated (right) NMR spectra of the olefinic carbons of *cis*-cyclononene. The rate constants shown are k_1 of eq 1.

Rate constants were obtained from the ^{13}C spectra by line shape matching with spectra calculated[12] with an IBM-compatible PC. The rate constant for the ^{1}H spectrum at −102.3 °C was calculated using an approximate equation, $k_C = (\pi/2^{1/2} \times \Delta\nu)$. The free-energy barriers were calculated from the Eyring equation with a program written by Newmark[13] and installed on an Apple computer.

The conformational space of **1** was searched by the grid-search technique with Allinger's MM3 program included in Spartan 3.0.[14] A total of 195 conformations were generated with the Osawa method and a grid step of 30°. Individual structures obtained in this way were used to prepare input for an external MM3 program[15] installed on a Silicon Graphics-IRIS workstation. Geometry optimization was accomplished by the block diagonal procedure followed by full matrix minimization, and harmonic vibrational frequencies were calculated. Relative strain energies, relative free energies at two temperatures, and populations were obtained. The relative strain energies were in good agreement with published results[9] for **1**.

The geometries determined for the first six conformations of **1** according to strain energies were used as starting points for the ab initio calculations. The Gaussian 94 series of programs[16] was used for full geometry optimization, initially at the HF/3-21G* level and then at the HF/6-311G* level, followed by calculation of vibrational frequencies by the

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[12] Calculated spectra were obtained using program DNMR–SIM, written by G. Hagele and R. Fuhler, Heinrich-Heine University, Dusseldorf Institute of Inorganic and Structural Chemistry, Dusseldorf, FRG, 1994.

[13] Newmark, R. A. *J. Chem. Educ.* **1983**, *60*, 45.

[14] Spartan Version 3.0 from Wavefunction, Inc., Irvine, CA.

[15] Version MM3 (94) was used. The latest version of the MM3 program, which is referred to as MM3 (96), is available to academic users from the Quantum Chemistry Program Exchange, and to commercial users from Tripos Associates, 1699 South Hanley St., St. Louis, MO 63144.

[16] Gaussian 94: Rev. E. 2, Frisch, M. J.; Trucks, G. W.; Gill, P. M. W.; Johnson, B. G.; Schlegel, H. B.; Robb, M. A.; Cheeseman, J. R.; Gomperts, R.; Keith, T.; Petersson, G. A.; Montgomary, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, J. V. O.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Fox, D. J.; Head-Gordon, M.; Binkley, J. S.; Gonzales, C.; Martin, R. L.; Defrees, D. J.; Baker, J.; Stewart, J. J.; Pople, J. A.; Gaussian, Inc., Pittsburgh, PA 1995.

Table 1. Parameters Used to Calculate Lineshapes for the ^{13}C Spectra of the Olefinic Carbons of *cis*-Cyclononene, and the Free-Energy Barriers Obtained

		populations		rate constants[a]			
temp (°C)	line width of TMS (Hz)	major	minor	k_1 (s^{-1})	$2k_2$ (s^{-1})	ΔG,$^{\ddagger\,b}$ kcal/mol	ΔG,$^{\ddagger\,c}$ kcal/mol
−178.3	9.0	0.60	0.40	228.0	342.0	4.31	4.23
−183.1	10.5	0.63	0.37	75.0	127.8	4.28	4.18
−184.8	10.9	0.64	0.36	30.5	54.2	4.35	4.25
−189.3	11.6	0.66	0.34	12.0	23.4	4.28	4.17
slow exchange	11.6	0.66	0.34	0.001	−	−	−
						4.31(ave)	4.21(ave)

[a] k_1 and k_2 are defined in eq 1. [b] Free-energy barrier for conversion of the major conformation to the minor conformation. [c] Free-energy barrier for conversion of the minor conformation to the major conformation.

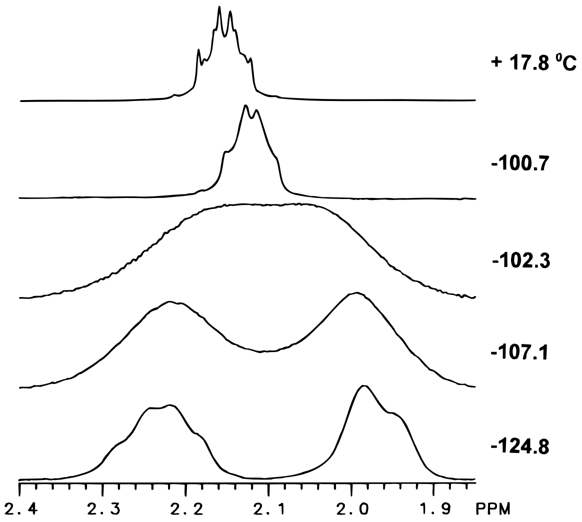


Figure 3. ^{1}H NMR spectra of *cis*-cyclononene in propane.

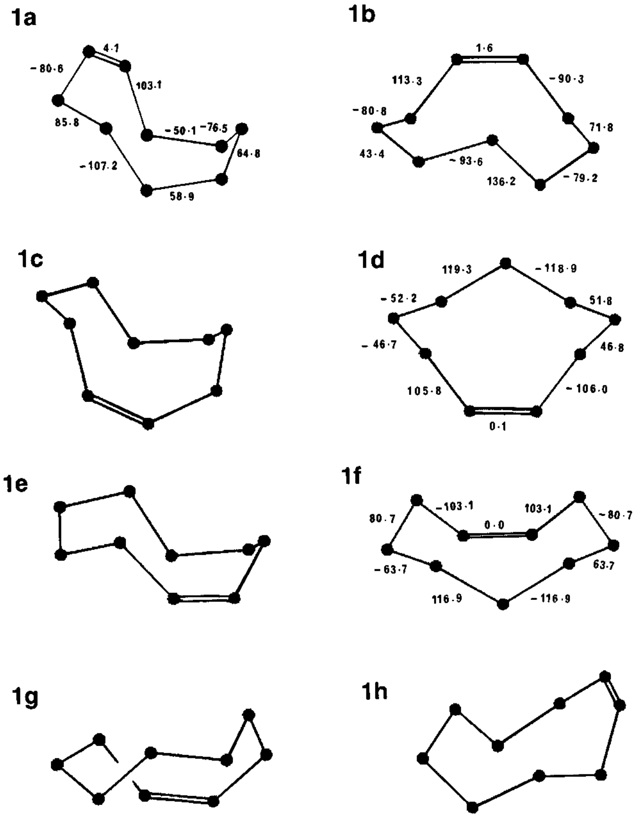


Figure 4. Conformations of *cis*-cyclononene in order of increasing MM3 strain energies. CCCC dihedral angles are shown for several of the conformations.

analytical method and calculation of thermodynamic properties. For the frequency calculations, the default scaling factor of 0.89 was used.

Results and Discussion

The ^{13}C spectrum of **1** at +17.8 °C shows the expected five peaks at δ 130.99 (C=C), 27.22, 26.93, 26.70 (C-6), and 26.45, relative to the carbons of internal TMS (Figure 1). The spectra change at lower temperatures, and three peaks at δ 131.25, 130.07, and 129.66 are observed at −189.3 °C in the olefinic region. The outer two peaks are assigned to a conformation of C_1 symmetry, and the central peak is associated with a minor conformation of C_s or time-averaged C_s symmetry. The eleven peaks found at lower frequency for the CH$_2$ carbons support these assignments; the peak at lowest frequency (δ 19.43) has about half the intensity of the other 10 signals and arises from C-6 of the conformation with C_s or time-averaged C_s symmetry.

Rate constants and populations were obtained from line shape matching of the olefinic carbon signals. The appearance of the spectra suggested that exchange of sites in the major C_1 conformation occurs by conversion to the minor conformation. The calculations were therefore based on eq 1, where A and A′ represent the

$$\mathrm{A} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{B} \underset{k_1}{\overset{k_2}{\rightleftharpoons}} \mathrm{A}' \qquad (1)$$

enantiomeric forms of the major conformation, and B is the minor conformation. Calculated and experimental spectra are shown in Figure 2, and the results are summarized in Table 1. For example, the populations of A, A′, and B at −183.1 °C were 0.315, 0.315, and 0.37, and k_1 and k_2 were 75.0 and 63.9 s^{-1}; the free-energy barrier for conversion of (A + A′) to B was calculated from the rate constant of 75.0 s^{-1} to be 4.28 kcal/mol, and the rate constant and barrier for the reverse process were 127.8 s^{-1} and 4.18 kcal/mol. The good agreement between calculated and experimental spectra provides strong support for the assumption that exchange of sites in the major conformation occurs by way of conversion to the minor conformation. The rate constants of 12.0 and 23.4 s^{-1} at −189.3 °C indicated that slow exchange has not been reached by this temperature. A spectrum calculated with an arbitrary small k_1 of 0.001 s^{-1} is included in Figure 2.

The proton NMR spectrum of the allylic hydrogens of **1** decoalesces at low temperatures into two multiplets of equal intensity, with coalescence at −102.3 °C and slow exchange by −124.8 °C (Figure 3). The observed changes are expected to be a consequence of slowing exchange

Table 2. Relative Strain Energies, Relative Free Energies, and Populations of Different Conformations of *cis*-Cyclononene, Calculated Using Allinger's MM3 Program

			25 °C		−189.3 °C	
conformer	symmetry	relative strain energies (kcal/mol)	relative free energies (kcal/mol)	populations	relative free energies (kcal/mol)	populations
1a	C_1	0.00	0.32	0.25	0.26	0.17
1b	C_1	0.03	0.00	0.42	0.00	0.80
1c	C_1	0.30	0.77	0.12	0.70	0.01
1d	C_s	0.69	1.01	0.08	0.82	0.00
1e	C_1	0.71	0.90	0.09	0.77	0.01
1f	C_s	0.78	1.57	0.03	0.75	0.01
1g	C_1	2.16	2.02	0.01	2.32	0.00
1h	C_1	3.92	3.95	0.00	3.96	0.00

Table 3. Relative Free Energies of Different Conformations of *cis*-Cyclononene from ab Initio Calculations at the HF/6-311G* Level

	relative free energies (kcal/mol)[a]			
conformer	25 °C	−189.3 °C	low frequency (cm^{-1})	symmetry
1a	0.00	0.00	118.454	C_1
1b	0.82	1.00	91.838	C_1[b]
1c	1.52	1.65	82.456	C_1
1d	1.36	1.43	116.156	C_s
1e	0.90	0.77	160.208	C_1
1f	1.61	1.25	59.035	C_s

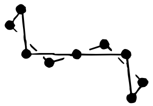
[a] The free energies calculated by Gaussian 94 have not been changed; the *R* ln 2 contribution to entropy for the enantiomers of the C_1 conformations is not included in Gaussian 94 and has not been added (see ref 6). [b] Although **1b** has C_1 symmetry, the deviation from C_s symmetry is small (see Figure 4 and text).

between the geminal hydrogens, and a free-energy barrier of 8.05 ± 0.2 kcal/mol was calculated for the process at coalescence.

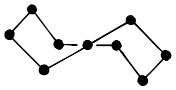
The conformations for **1** predicted by Allinger's MM3 program are shown in Figure 4, and the symmetries, relative strain energies, relative free energies, and populations are listed in Table 2. The results of ab initio calculations at the HF/6-311G* level are given in Table 3. Conformations **1d** and **1f** have C_s symmetry, and the other six conformations of Table 2 are of C_1 symmetry. However, conformation **1b** has a strong resemblence to the plane-symmetrical conformation **1f**, and the free energy difference between them at −189.3 °C is small by either MM3 or HF/6-311G* (0.75 or 1.25 kcal/mol). If the barriers to interconversion of these two conformations are also low, then **1b** could have time-averaged C_s symmetry at the temperatures of the experimental study.

Conformation **1a** has the lowest free energy at −189.3 °C according to the ab initio calculations and the second-lowest energy by MM3 (only 0.26 kcal/mol above **1b**). On the basis of these calculations and the symmetry determined by the ^{13}C NMR study, the major conformation of **1** is suggested to be **1a**. Of the possible assignments for the minor conformation (**1b**, **1d**, and **1f**), **1b** has the lowest calculated free energy at −189.3 °C by both MM3 and HF/6-311G*. The possibility that other C_1 conformations (**1c** and **1e**) may have barriers to racemization low enough to have time-averaged C_s symmetry at −189.3 °C cannot be completely excluded, and the calculated free energies of **1d** and **1f** are not sufficiently high for these conformations to be entirely eliminated from consideration, but at present the most likely candidate for the minor conformation of **1** is **1b**.

The major conformation (95%) of cyclononane at −173 °C was reported[17] in a low-temperature NMR study to be the [333] conformation (**2a**), which has D_3 symmetry, and the C_2 conformation [225] (**2b**) was suggested to account for the other 5% at this temperature. Evidence was described[17] for a third conformation at higher temperatures, the [144], with an estimated population of only about 1% at −95 °C. Molecular mechanics calculations have also been carried out for cyclononane with several force fields, including a force field of Boyd,[17,18] MM2,[18,19] MM3,[19] and MM4.[20] An X-ray study[21] of cyclononylamine hydrobromide found two conformations in the solid state, each of which had the [225] ring conformation, but differing in the position of the substituent on the ring. Conformations **1a** and **1b** of *cis*-cyclononene do not resemble **2a** or **2b** of cyclononane, and the preferred conformations of **1** appear not to be based on the low-energy conformations of cyclononane.



2a



2b

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